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| NORRIS, MCLAUGHLIN & MARCUS, P.A. | | | EXAMINER | |
| 875 THIRD AVE | | | SHEN, BIN | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/516,441

Applicant(s)

IRTH ET AL.

Examiner

Bin Shen

Art Unit

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

The IDS received 2/14/2005, the preliminary amendment received 11/30/2004 have been entered.

Claims 1-13 are presented for examination on the merits.

Specification

1. The abstract of the disclosure is objected to because the abstract must be a single paragraph. Correction is required. See MPEP § 608.01(b). A new abstract on a separate page is required to replace the current abstract, which is the first page of the WO document of the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

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the application was filed, had possession of the claimed invention.

Claim 13 refer to a compound without giving a true technical characterization. Moreover, no such specific compound is defined in the specification. No structural or specific functional characteristics of such compound is provided, nor is there any indication that the applicant had possession of the claimed compound. One skilled in the art would conclude that the inventors were not in possession of the claimed invention, the claims fails to comply with the written description requirement. Further, since this Examiner cannot determine what compound is claimed, it cannot be searched.

3. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to disclose any particular structure for the claimed compound. The specification does not provide any guidance or any working examples in this unpredictable art, and thus the artisan would have been unable to prepare the claimed compound. Furthermore, a method for detecting a compound is not equivalent to a positive recitation of how to make a product. The claims fail to meet the enablement requirement for the "how to make" prong of 35 U.S.C. 112, first paragraph. Thus, the skilled artisan would not been able to make and use the compositions as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 8 recites the limitation "separation step" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 4, 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Ingkaninan et al. (J Chromatography 2000;872:61-73).

Ingkaninan et al. teach an on-line detection method for inhibitors of enzymes and their inhibition activity, comprising the steps of: contacting a fractionation effluent with a controlled amount of an enzyme (Acetylcholinesterase-AchE); allowing the enzyme to interact with analytes suspected to be present in the fractionation effluent; addition of a controlled

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amount of a substrate for the enzyme; allowing a reaction of the enzyme with the substrate providing one or more modified substrate products; and detection of unreacted substrate or a modified substrate product using and UV-Vis spectrometer and detection of the inhibitor using a mass spectrometer (see abstract; page 64, Fig. 1c; page 67, left column, line 7; page 70, right column, line 3), and the fractionation step is a high-performance liquid chromatography (HPLC) (abstract).

Therefore, the cited reference is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-4, 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ingkaninan in view of Bocchini et al. (Rapid commun Mass Spectrom 1999;13(20):2049-2053).

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Ingkaninan teach what is above.

Ingkaninan does not teach the passage of the reaction mixture through a hollow-fibre module prior to entering the mass spectrometer.

Bocchini et al. teach the use of a thin polymeric hollow-fibre membrane for the reaction mixture to pass through prior to entering the mass spectrometer (abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the hollow-fibre membrane in the method of Ingkaninan because Bocchini teaches the advantages of the technique are that no pretreatment of samples before analysis is needed and that it has fast response times and on-line monitoring capabilities. One would have been motivated to make the modification because Bocchini et al. specifically described the set-up of the system (hollow-fibre module) and the evaluation of the linearity of response, repeatability, detection limits, and spectra quality, and would reasonably have expected success in view of both Ingkaninan and Bocchini's teachings.

7. Claims 1, 2, 4-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ingkaninan in view of Edmondson et al. (Molecular & Cellular Proteomics 2002;1:421-433).

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Ingkaninan teach what is above.

Ingkaninan does not teach the use of electrospray ionization mass spectrometry, and the adding of a make-up flow to the reaction mixture, and the mixture of two or more enzymes (one of the enzyme is a protein kinase), and a mass spectrometer with a multiple-inlet.

Edmondson et al. teach the use of a ionization mass spectrometry to identify many proteins in Protein Kinase C (PKC) ϵ complex (abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use ionization mass spectrometry to identify multiple enzymes (proteins) in the method of Ingkaninan because Edmondson teaches that identifying the protein components of the protein complexes (such as PKC ϵ) is important for understanding its physiological function (abstract and page 421, right column, 1st paragraph). One would have been motivated to make the modification because Edmondson specifically described a mass spectrometry analysis with fast gradient nanoscale LC/MS/MS with splitting streams (read as multiple-inlet) (page 423, right column 1st full paragraph), and the mixture of peptides (proteins) are analyzed using electrospray tandem mass spectrometers (page 424, left column 1st full paragraph), and would reasonably have expected success because Edmondson teaches that the method they use are highly sensitive (abstract, lines 16-18). The adjustment of particular conventional working conditions (e.g., electrolyte pH, make-up chemical composition and make-up flow-rate) is deemed merely a matter of judicious selection and routine optimization, which is well within the purview of the skilled artisan having the cited reference before him/her.

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From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

8. No claim is allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application

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Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, Ph.D., whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday

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through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Terry McKelvey can be reached at (571) 272-0775.



MICHAEL MELLER
PRIMARY EXAMINER

B Shen

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